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The presence of serum autoantibodies and donor-specific anti-HLA antibodies in pediatric liver transplant recipients is associated with histological and biochemical parameters of graft dysfunction

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Objectives and Study: Serum autoantibodies (AAb) as well as donor-specific anti-HLA Ab (DSA) are frequently present in pediatric liver transplant (LT) recipients. Their clinical significance remains incompletely understood when encountered outside the context of de novo autoimmune hepatitis (AIH). We aimed to study the prevalence of serum AAb and DSA in pediatric LT recipients under follow-up at Ghent University Hospital and investigate their correlation with patient characteristics and clinical outcome in terms of histological and biochemical parameters.

Methods: Based on electronic patient data, we retrospectively collected the data on AAb (antinuclear factor, ANF; anti-smooth muscle Ab, ASMA; anti-soluble liver antigen Ab; anti-liver cytosol type 1 Ab; anti-liver kidney microsomal Ab) and DSA in 62 pediatric LT recipients (median age 3,8 y; range 0,1-17,1 y; 37 male) under follow-up at Ghent University Hospital between january 2007 and february 2018. The patient characteristics (age, sex, age at LT, time of follow-up, LT indication, donor type and age, need for retransplant or death), need for liver biopsy (LB) and number of LB, histological findings (acute cellular rejection; chronic rejection; histological signs suggestive of biliary obstruction; de novo AIH; idiopathic post transplant hepatitis (IPTH); aspecific alterations and steatosis) and biochemical parameters (Alkaline Phosphatase, AP; ALT; AST; γ-GT; total and direct bilirubin; albumin; thrombocyte count; Immunoglobulin G; EBV and CMV DNA) were registered at several time points (year 1, 3, 5, 10 and 15) post LT. Statistical analysis was performed using SPSS Statistics (version 25).

Results: AAb were detected in 27 (43,3%) patients, with ANF being the most frequently encounterd AAb in 15 (24,2%) patients followed by ASMA in 13 (21%) patients. There was a positive correlation between AAb positivity and female gender (p=0,032) and cadaveric LT (p=0,006). In 54 patients at least one liver biopsy was performed during their post-transplant course. Acute cellular rejection was present in 20 (32%), chronic rejection in 7 (11%), histological signs of biliary obstruction in 16 (25%), de novo AIH in 4 (6,5%), aspecific histological changes in 25 (40%), IPTH in 5 (8,1%) and steatosis in 12 (19%) patients. Patients with positive AAb underwent a higher number of LB during their follow-up (p< 0,001) and in the absence of de novo AIH, an association was found with the presence of aspecific histologic alterations (p=0,032). Outside the context of de novo AIH, positive AAb were associated with increased AP (p< 0,001), ALT (p< 0,001), AST (p< 0,001), γ-GT (p=0,001), IgG (p=0,007) and decreased albumin (p=0,029). 14 out of 50 patients were DSA positive (all anti-HLA class II). DSA positivity was associated with acute cellular rejection (p=0,019), increased direct bilirubin (p=0,033) and γ-GT (p< 0,001).

Conclusions: The presence of AAb in the absence of de novo AIH as well as DSA positivity is associated with histological and biochemical parameters of graft dysfunction. Larger prospective studies are warranted to further investigate the causal relationships between AAb and DSA development and outcome parameters post pediatric LT.

Disclosure of interest: -

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